25. (Amended) The isolated polypeptide of Claim 24 comprising amino acid residues about 1 to about 577 of SEQ ID NO:2.

26. (Amended) An isolated polypeptide having at least about 80% sequence identity to the polypeptide encoded by the cDNA insert of the vector deposited with the ATCC as Deposit No. PTA-799.

27. (Amended) The isolated polypeptide of Claim 26 which is encoded by the cDNA insert of the vector deposited with the ATCC as Deposit No. PTA-799.

28. (Amended) An isolated polypeptide scoring at least 80% positives when compared to the sequence of amino acid residues from about 1 to about 577 of SEQ ID NO:2.

29. (Amended) An isolated polypeptide comprising the sequence of amino acid residues from about 1 to about 577 of SEQ ID NO:2, or a fragment of the polypeptide sufficient to provide binding for an antibody capable of specifically binding to said isolated polypeptide.

30. (Amended) An isolated polypeptide produced by a method comprising (i) culturing a host cell comprising a DNA molecule under conditions suitable for expression of the polypeptide, wherein said DNA molecule is capable of hybridizing under stringent conditions with (a) a DNA molecule encoding a polypeptide comprising the sequence of amino acid residues from about 1 to about 577 of SEQ ID NO:2, or (b) the complement of the DNA molecule of (a); and (ii) recovering the polypeptide from the cell culture.

32. (Amended) A chimeric molecule comprising a polypeptide of SEQ ID NO:2 fused to a heterologous amino acid sequence.

60. (Amended) A composition comprising a polypeptide of SEQ ID NO:2 in admixture with a pharmaceutically acceptable carrier.

61. (Amended) The composition of Claim 60 comprising a therapeutically effective amount of a polypeptide of SEQ ID NO:2.

67. (Amended) A method of preparing the composition of Claim 60 comprising admixing a polypeptide of SEQ ID NO:2 with a pharmaceutically acceptable carrier.

SUPPORT FOR AMENDMENTS

Support for the amendments can be found in the original claims 24-30, 32, 60 and 67. No new matter has been added. Claims 24-35, 60-62 and 67 are now present and pending in the application.

A marked-up version of the amended claims (Appendix A) is attached; [brackets] indicate deleted material; underlining indicates added material. Also provided in Appendix B is a clean copy of all pending claims for the Office's convenience.

IN THE SPECIFICATION

A Substitute Specification has been supplied to correct the placement of the computer program listing. The program listing has been moved from old pages 19-35 to new pages 130-150, immediately preceding the claims. No new matter has been added and no matter has been deleted. The difference in the number of pages are accounted for by changes in formatting that were necessary to accommodate the available printers.

A red-lined copy of the specification indicating changes has been provided.

DECLARATION

Applicants thank the Office for indicating the defective Declarations. New Declarations in compliance with 37 CFR §1.67(a) identifying this and the provisional application by application numbers and filing dates will be provided when they become available.

REQUEST FOR RECONSIDERATION

The growth of new vessels from pre-existing vessels--angiogenesis--is an important biological process, both for homeostasis and disease conditions. Angiogenesis is a complex phenomenon that takes place in distinct phases that entails and relies upon modulation or expression of a variety of intracellular proteins, extracellular matrix components, proteases, inflammatory molecules, chemokines, and molecules involved in cell division and proliferation, cytoskeletal rearrangement, adhesion and apoptosis.

In a variety of diseases and disorders, including tumor growth and metastasis, endothelial cells undergo angiogenesis during neovascularization. For example, in tumor growth, angiogenesis appears to be crucial for the transition from hyperplasia to neoplasia, and for providing nourishment to growing solid tumors. Angiogenesis also allows tumor cells access to the circulation system of the host, providing a route for metastasis. Thus one route of controlling tumor growth and metastasis is preventing or reducing neovascularization in tumors, which can be accomplished by using molecules that discourage angiogenesis. In conditions such as cardiac infarction or congestive heart failure, cardiac blood vessels are lost. To aid in repairing the damage that these and other conditions incur, molecules that encourage angiogenesis are desirable. This invention provides a molecule associated with angiogenesis that can be used in such treatments.

Claim Rejections 35 USC 101

The rejection of claims 24-35, 60-63, and 66-67 is respectfully traversed. The claimed invention meets all of the requirements for credible, substantial and specific utility. The PRO-C-MG.2 polypeptide (SEQ ID NO:2) is associated with angiogenesis.

The utility is credible: PRO-C-MG.2 is up-regulated during angiogenesis, indicating that this gene is important in neovascularization. The specification teaches that the PRO-C-MG.2 polypeptide is involved, for example, in the neovascularization of tumors, among other conditions (*e.g.*, p. 28, line 12-p. 29, line 2). The utility of PRO-C-MG.2 is also revealed in the experimental design. Using an art-accepted model system of angiogenesis (Davis & Camarillo 1996, Dentelli *et al.*, 1999, Ilan *et al.*, 1998, Juarez *et al.*, 2002, Soeda *et al.*, 2002, Xin *et al.*, 1999); references enclosed herewith), it has been determined that during angiogenesis, PRO-C-MG.2 is up-regulated. Because PRO-C-MG.2 expression is up-regulated *during* angiogenesis, this molecule is associated with, and likely promotes vascularization.

The utility of the invention is specific: the specificity of the discovered sequence is built into the experimental design--PRO-C-MG.2 expression relates to angiogenesis because it is up-regulated in an art-accepted model of angiogenesis. The importance of angiogenesis in wound repair after, for example, cardiac infarction, congestive heart failure, or ischemia, is critical for rescue and repair of the affected tissues. The need to detect presence and/or extent of angiogenesis in diseases such as cancer is also evident to one skilled in the art in view of the importance of angiogenesis as a disease promoting process. Pro-C-MG.2 represents a novel

molecule closely associated with the process of angiogenesis, and thus serves as a novel target for detection, diagnosis and/or therapy.

The utility is substantial: PRO-C-MG.2 has a real life utility. Conditions and disease that damage and kill blood vessels, such as found in myocardial infarctions, congestive heart failure, ischemia and other conditions that involve wound healing, not only reduce the quality of life of the victims, but also kills thousands annually. Therefore, the claimed polypeptide has a utility in detection and diagnosis of conditions associated with wound healing or angiogenesis.

The significant increase in gene expression of PRO-C-MG.2 was observed in the context of cells that were specifically induced to undergo angiogenesis, the increase in expression being measured relative to a set of cells that differed from the PRO-C-MG.2-expressing cells only in that they were not similarly induced (and thus were not capable of undergoing angiogenesis). Thus, one of skill in the art would not view the significant difference in expression levels between these two sets of cells, as saying "nothing about the purported biological properties of the PRO-C-MG.2 polypeptide." Applicants respectfully submit that the logic and facts as offered in the specification and in view of art teachings, and the tight association of PRO-C-MG.2 expression with the process of angiogenesis, support a credible and specific utility. As noted in the specification and above, PRO-C-MG.2 has various utilities, for example as a therapeutic agent, and as a target for detection, diagnosis and/or therapy.

Concerns have been raised about the uncertainty of mRNA is translation. The norm is that mRNA is translated soon after transcription. Exceptions exist, but these are just that: exceptions. Alberts, *et al.* (Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts, P. Walter 2002; included herewith) indicate that post-transcriptional controls, while being one way of regulating translation, are not the norm. On page 435, Alberts, *et al.* note, "controls on the initiation of gene transcription are the *predominant* form of regulation for *most* genes" (emphasis added). There is no evidence that PRO-C-MG.2 is an exception to the rule that genes are regulated transcriptionally.

Thus the invention meets the criteria of 35 USC §101. Because the utility requirements are met, one of skill in the art would know how to use the invention. Applicants respectfully request withdrawal of the rejections made under 35 USC §101 and 35 USC § 112, first paragraph.

Claim Rejections 35 USC §112, first paragraph

The rejections of claims 24-35, 60-63, 66-67 under 35 USC § 112, first paragraph, is respectfully traversed. The Applicants had possession of the claimed invention, at the time of filing.

A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented (MPEP § 2163.04, p.2100-168 (August 2001); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)). Compliance with the written description requirement does not require an applicant to describe exactly the subject matter claimed; rather, the description must allow one of ordinary skill in the art to recognize that the applicant has invented what is claimed (MPEP § 2163.02, p. 2100-167 (August 2001); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989); *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991)). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials (*Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997)). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. *Id.* at 1406. One of skill in the art would have recognized, at the time of filing of the instant application, that Applicants were in possession of the claimed polypeptides.

The Applicants have provided such a formula. Firstly, the sequence of PRO-C-MG.2 is given in SEQ ID NO:2. Furthermore, an art-accepted method for calculating sequence identity has also been provided (page 16, line 5 to page 19, line 18). The specification specifically teaches variants of SEQ ID NO:2; for example, see line page 35, line 18 to page 36 line 19 (chimeric and fusion polypeptides comprising the polypeptide sequence of SEQ ID NO:2) and page 31, line 36 to page 32, line 15 for variants wherein conservative amino acid substitutions have been made.

The instant specification would convey with clarity to those skilled in the art that, as of the filing date, Applicants were in possession of the claimed subject matter. The law, as articulated by the Federal Circuit, requires no more. *See, Vas-Cath Inc v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Thus, applicants respectfully request the Office to withdraw this basis for rejection under 35 USC § 112, first paragraph.

Claim Rejections 35 USC §112, second paragraph

The rejections of claims 26-27, 32-35, 60-63, and 66-67 have been obviated by appropriate amendment.

Claim Objections

The objections to claims 24-35, 60-63 and 66-67 have been obviated by appropriate amendment.

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